

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of :
Andreas SEWING et al. : Group Art Unit: 1616
Serial No.: 09/885,287 : Examiner: Gollamudi S
Filed: June 21, 2001:
For: COATING FOR METALLIC IMPLANT MATERIALS

Pre-Appeal Brief Request For Review

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

SIR:

In response to the Office Action of February 8, 2008 and prior to the filing of an Appeal Brief please consider the remarks that follow.

The Examiner continues to cite the Webster dictionary definition of “mineralize”, despite the inventors meaning of the phrase “mineralized collagen matrix”, which is clear from the intrinsic record. Applicants may be their own lexicographer and need not explicitly define a term or phrase. The first line of Applicants specification states: “ The invention relates to a biomimetically produced bone analogous coating...” As pointed out on page 3, lines 4-12 of the specification in reference to the prior art: “Methods which comprise both hydroxyapatite and collagen are only restricted to mixtures of the components....”. The implication is clear. The specification teaches a skilled worker that the mineralized collagen matrix according to the invention is not a simple mixture of hydroxyapatite and collagen, like the prior art, but is instead is biomimetically produced and bone analogous.

It is clear from Applicants specification (and the claim language) that the matrix is biomimetically produced from an electrolyte solution. See page 4 line 39-40 of the specification. Furthermore, the mineralized collagen matrix is in the form of layers. See page 5, line 15-19 and the claim language. Electron microscope examination, X-ray diffraction investigations and IR-spectroscopic investigations are used to characterize these layers. See examples 1-4. Furthermore, as seen on page 11 of the specification, the collagen is not present in denatured form, but on the contrary a good agreement exists

between the mineralized layer and a spectrum from native bone. Thus, the mineralized collagen matrix is constructed in the form of layers. At least one of the layers comprises a composite of mineralized collagen fibrils, amorphous calcium phosphate clusters and crystalline hydroxyapatite. Crystals of hydroxyapatite having a length of about 300 to 500 nm are present on and between the collagen fibrils.

Contrary to the Examiners assertion on page 7, line 16 of the Office Action, Applicants need not explicitly define a term or phrase. As stated in the MPEP at section 2111.01 (IV), the specification should also be relied on for more than just explicit lexicography or clear disavowal of claim scope to determine the meaning of a claim term when applicant acts as his or her own lexicographer; the meaning of a particular claim term may be defined by implication, that is, according to the usage of the term in the *context* in the specification. See *Phillips v. AWH Corp.*, 415 F.3d 1303, 75 USPQ2d 1321 (Fed. Cir. 2005) (*en banc*); and *Vitronics Corp. v. Conceptronic Inc.*, 90 F.3d 1576, 1583, 39 USPQ2d 1573, 1577 (Fed. Cir. 1996). Applicant's have clearly defined "mineralized collagen matrix". It has been consistently used in the context of "bone analogous coating" and in the form of layers produced biomimetically from an electrolyte solution.

In construing claim terms, the general meanings gleaned from reference sources, such as dictionaries, must always be compared against the use of the terms in context, and the intrinsic record must always be consulted to identify which of the different possible dictionary meanings is most consistent with the use of the words by the inventor. See *ACTV, Inc. v. The Walt Disney Company*, 346 F.3d 1082, 1092, 68 USPQ2d 1516, 1524 (Fed. Cir. 2003). Absent an express definition in the specification a term should be given its broadest reasonable interpretation consistent with the intrinsic record and take on the ordinary and customary meaning attributed to it by those of ordinary skill in the art. See *E-Pass Technologies, Inc. v. 3Com Corporation*, 343 F.3d 1364, 1368, 67 USPQ2d 1947, 1949 (Fed. Cir. 2003).

On page 8, line 5 of the Office Action the Examiner cites Du et al. The Du reference further supports Applicants' position that the term "mineralized collagen matrix" does not mean a simple admixture as the Examiner alleges. At page 519, Col. 1 it is stated:

"Natural bone is a complex biomineralized system with an intricate hierarchical structure.⁹ It is assembled through the orderly deposition of apatite minerals within a type I collagenous organic matrix."

Du et al. goes on to describe the hydroxyapatite crystals that grow on the collagen fibrils. The naturally given size of a collagen fibril is about 3000 Å. See page 173 of Lehninger "Principles of Biochemistry" previously provided and discussed on page 7 of the August 2006 response. Therefore, hydroxyapatite crystals formed on the fibrils cannot be larger than the size of a collagen fibril, i.e. 300 to 500 nm. The size of the hydroxyapatite crystals according to claim 1 is between 300 to 500 nm. Due to the applied electrochemical process the crystals cannot be larger than that. The Du et al. reference further teaches a skilled worker that mineralized collagen is a common scientific term, and it is not a simple mixture. A key step in Du's mineralization process is the growth of calcium phosphate minerals on a collagen matrix in aqueous media (page 519, left column, third paragraph). Additionally, Du et al. teaches that mineralized collagen as bone analogous material can only be obtained under precise reaction conditions. According to Du et al. the preferred approach for obtaining a mineralized collagen comprises soaking a collagen matrix in a phosphate solution with a pH of 14 (solution B) followed by immersing in a calcium chloride solution (solution A, page 520, right column, first paragraph). Under Du, a very specific step of sequences is used to provide a mineralized collagen matrix.

Applicants note however that the membrane of Du cannot be used in an electrochemical process due to a lack of electrical charges on the membrane surface. Furthermore, the formation of calcium phosphate on the collagen fibrils and the subsequent washing removes all charged particles from the membrane (page 525, left column, second paragraph of Du et al.).

Thus, a skilled worker would recognize from Du et al. that achieving a mineralized collagen matrix requires very specific conditions to. It is not a simple admixture of hydroxyapatite and collagen.

The Examiner cites a multitude of references to make various obviousness rejections. However, even piecing these references together in hindsight reconstruction does not arrive at the present invention. The mineralized collagen matrix of the present invention is constructed in the form of layers, whereby at least one of said layers comprises a composite of mineralized collagen fibrils, amorphous calcium phosphate and crystalline hydroxyapatite, wherein the crystals of said crystalline hydroxyapatite have a length of about 300 to 500 nm. This alone establishes patentability of the claimed invention. However, as noted in the first line of the specification the bone analogous coating is biomimetically

produced. Thus, in the interest of furthering prosecution, Applicants amended the claims to include the process of preparing the biomimetically coated implant. Thus, Applicants have distinguished the implant of the present invention from the prior art products not only in terms of composition and/or structure but also by the unique process of making. As can be seen in related continuation application 10/414,284 (now US 7,229,545) the USPTO determined that the process of making the implant of the present invention was patentable. Thus, none of the cited prior art teaches the process of making the coating of the present invention.

On page 8 of the Office Action, the Examiner alleges that the Applicants have not provided evidence establishing an unobvious difference between the claimed product and prior art product. The Examiner has provided no evidence other than mere speculation, that the product of the prior art is identical to the product of the present invention. It is clear from the record that the process limitations, now claimed, impart a structurally defining feature to the coating of the claimed invention. In addition to the Examples in the specification, which provide electron microscope examinations, X-ray diffraction investigations and IR-spectroscopic investigations to characterize the claimed invention, Applicant has previously provided evidence establishing an unobvious difference between the claimed product and the prior art products. For example, in the response dated 31 October 2007 Applicants presented the spectrum from native bone and compared it to a mineralized collagen matrix according to the invention. The spectrum from simple mixtures of hydroxyapatite and collagen are also presented. Thus, Applicants have shown that the process of making the coating according to the invention results in a clear physical distinction from the products of the prior art.

Neither JP '259, Constanz, Lussi et al., Sauk, Geistlich, Shirkanzedah, Worsch nor Liu et al., (the structural differences have previously been discussed in detail in every response of record) disclose or suggest a mineralized collagen matrix constructed in the form of layers, whereby at least one of said layers comprises a composite of mineralized collagen fibrils, amorphous calcium phosphate and crystalline hydroxyapatite, and wherein the crystals of the crystalline hydroxyapatite have a length of about 300 to 500 nm. Furthermore, Lussi et al., who uses purified native bone particles, teaches away from selecting the particle size of the instant invention (See pages 13-14 of the May 2007 response). The references of record are particularly silent with respect to use of cathodic polarization in the coating process.

A multilayer coating is a structurally defined feature of the present invention and a clear physical distinction from the prior art.

As discussed above, a mineralized collagen matrix (according to the invention) has a structure that is bone analogous and thus, different from a simple mixture of calcium phosphate and collagen. Based on the above remarks and the remarks of record it is respectfully requested that the rejections under 35 USC §103 be withdrawn.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,
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Filed: 8 June 2008

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